REMARKS

Upon entry of the present amendment, claims 1-3, 5-9, 39, 40, 43-46, 51, 52, and 55-59 are pending in the application, claims 4, 41, 42, 44, 47, 50, 53, 54, 60, and 61 having been canceled by the present amendment. Applicants acknowledge the allowability of claim 57. Claims 7, 8, 40, 45, 55, 56, and 59 were amended to add ATCC deposit designations. Claim 40 was amended for clarity and to change claim dependency.

The specification was amended to add ATCC deposit information regarding antibody-producing hybridoma cell lines.

No new matter has been added.

I. Rejections under 35 U.S.C. § 102

Claims 41, 42, 44, 53, 54, 60, and 61 were rejected for anticipation by De la Monte et al. Claims 41, 42, 44, 53, 54, 60, and 61; therefore, this rejection can now be withdrawn.

Claim 45 was rejected for anticipation by Lavaissiere et al. This claim has been amended to require specific antibodies that were not described by the Lavaissiere et al. reference. Therefore, the amended claim is not anticipated by Lavaissiere et al.

I. Rejections under 35 U.S.C. § 103

Claim 49 was rejected for obviousness over De la Monte et al. in view of Huse et al., and claim 50 was rejected for obviousness over De le Monte et al. in view of Lavaissiere et al. This rejection should be withdrawn in view of the cancelation of claims 49 and 50.

III. Rejections under 35 U.S.C. §112, first paragraph

Claims 55 and 56 were rejected for lack of enablement. The Examiner states:

> The specification does not provide a repeatable method for obtaining the antibodies produced by the cell lines of claim 55, and they do not appear to be readily available material. Deposit of the cell lines would satisfy the enablement requirements of 35 U.S.C. 112.

Claims 55 and 56 have been amended to identify antibody-producing hybridoma cell lines, which were deposited with the ATCC. A copy of the ATCC deposit receipt is submitted herewith (Attachment A).

The rejection of claims 1-9 and 39, 40, 43, 46, 51, and 52 for lack of enablement was maintained. The Examiner alleges that the method is unpredictable based on data presented in

the Declaration of Michael S. Lebowitz, which was filed on August 7, 2002. At page 3, lines 11-22, of Paper No. 10, the Examiner states:

> As for Applicant's argument that an increase in HAAH level in bodily fluid correlates with a diagnosis of malignancy is not convincing because the data in Table 1 at page 2 of Dr. Lebowitz's declaration filed 8-13-2002 shows that HAAH is positive in bodily fluid samples of more than 6 percent of normal non-cancerous control while HAAH is negative in bodily fluid samples of 30 percent of breast cancer patients. Considering the state of art unpredictability of using a biomarker in bodily fluid for cancer diagnostic marker as demonstrated by Weg-Remers et al. and Teillac et al. (cited in the previous Office Action), limited teaching of the specification, and unpredictability of cancer detection using HAAH detected in bodily fluid in Dr. Lebowitz's declaration, it is maintained that one skilled in the art would have reasons to question the efficacy of the claimed method for cancer diagnosis and required undue experimentation involving analysis of a large amount of clinical samples.

Applicants submit that the specification coupled with the knowledge in the art of diagnostic medicine fulfills the requirements of §112 and that the skilled practioner would not have to resort to undue experimentation to practice the claimed invention.

The enablement standard requires that the specification provide a description that, when coupled with the knowledge possessed by a person of ordinary skill in the art, enables that person to make and use the claimed invention. Enablement is not precluded by the necessity for some experimentation; however, any required experimentation must not be undue experimentation. With respect to efficacy, the standard is that reasonable correlation between evidence and the asserted utility is sufficient.

Despite the Examiner's criticism of the data in Table 1 of Dr. Lebowitz's declaration of August 7, 2002, the data establish a reasonable correlation between an increase in HAAH level in a bodily fluid and a diagnosis of cancer. Moreover, many more clinical samples of bodily fluid have now been tested. The additional data is summarized in the accompanying Declaration of Dr. Michael Lebowitz. An expanded panel of human sera from both cancer patients and normal control individuals was tested using antibodies that bind to HAAH. The panel included 85 sera from individuals, who had been diagnosed with cancer, and 230 sera from individuals lacking a diagnosis of cancer. In 223 of the 230 non-cancerous (normal) serum samples, no HAAH was detected by the assay. The specificity of the assay was found to be 97%. The overall sensitivity of the assay for detection of cancer relative to non-cancer (normal) was 94%. The sensitivity of the assay is well within the range of clinically acceptable parameters for diagnosing disease, and in fact, is better than that associated with many other tumor markers.

The data described in the specification and in both of Dr. Lebowitz's declarations indicate that malignant neoplasms are reliably diagnosed by detecting an increase of HAAH in a bodily fluid compared to non-cancerous (normal) values using an antibody which binds to HAAH. Given the high specificity and sensitivity of the claimed diagnostic assay, undue experimentation would not be required to practice the invention. Applicants respectfully request withdrawal of this rejection.

CONCLUSION

Applicants submit that the application is in condition for allowance and such action is respectfully requested.

A petition for extension of time and a check in the amount of $930.00 is enclosed to cover the petition fee for a three month extension of time pursuant to 37 C.F.R. § 1.17(a)(3). The Commissioner is hereby authorized to charge any fees that may be due, or credit any overpayment of same, to Deposit Account No. 50-0311, Reference No. 21486-032. A Request for Continued Examination is filed herewith.

Should any questions or issues arise concerning the application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

IABeattie

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Dated: September 26, 2003

TRA 1821912v1

Express Mail Lable No. EV320186320US
Date of Deposit: Septemb[redacted]26, 2003

Attorney Docket No. 21486-032DIV1

ATCC

10801 University Blvd • Manassas, VA 20110-2209 • Telephone: 703-365-2700 • FAX: 703-365-2745

BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF
THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3
AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.2

To: (Name and Address of Depositor or Attorney)

Rhode Island Hospital
Attn: Jack R. Wands, MD
Liver Research Center
55 Claverick Street, 4th Floor
Providence, RI 02903

Deposited on Behalf of: Rhode Island Hospital

Identification Reference by Depositor:	**Patent Deposit Designation**
Mouse hybridoma cell line: HA15C7A	PTA-3383
Mouse hybridoma cell line: HA219B	PTA-3384
Mouse hybridoma cell line: HA386A	PTA-3385
Mouse hybridoma cell line: FB501	PTA-3386

The deposits were accompanied by: __ a scientific description _ a proposed taxonomic description indicated above. The deposits were received May 17, 2001 by this International Depository Authority and have been accepted.

AT YOUR REQUEST: X We will inform you of requests for the strains for 30 years.

The strains will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strains, and ATCC is instructed by the United States Patent & Trademark Office or the depositor to release said strains.

If the cultures should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace them with living cultures of the same.

The strains will be maintained for a period of at least 30 years from date of deposit, or five years after the most recent request for a sample, whichever is longer. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the cultures cited above was tested May 30, 2001. On that date, the cultures were viable.

International Depository Authority: American Type Culture Collection, Manassas, VA 20110-2209 USA.

Signature of person having authority to represent ATCC:

Tanya Nunnally, Patent Specialist, Patent Depository

Date: June 27, 2001

cc: Ingrid Beattie
(Ref: Docket or Case No.: 21486-032)

RP49

Attachment "A"